

In the Claims:

Please amend claim 9 as follows:

1.(withdrawn) A method of *in vitro* screening for a ligand including selecting said ligand by means of at least two assay systems, said method comprising the steps of:

a) in a cellular or tissue assay system comprising an estrogen receptor and an estrogen receptor-driven reporter gene, selecting the ligand having a transcriptional activity mediated by activation of the estrogen receptor and measured by detecting a potency in the cellular or tissue assay system, whereby in the cellular or tissue assay system the ligand activates the potency with a half-maximally effective ligand concentration

(EC₅₀(ER)) less than or equal to 10 nmol/l, and

detecting the activation of the transcription;

and

b) in a cell-free or enzymatic assay system, selecting a physical-chemical interaction of a co-present steroid receptor coactivator-1, and fragments thereof, and the estrogen receptor, which is measured by detecting a potency of said interaction in the cell-free or enzymatic system, wherein the ligand activates the estrogen receptor and induces said interaction with said co-present steroid receptor coactivator-1, and fragments thereof, in the cell-free or enzymatic assay system with a half-

maximally effective ligand concentration ($EC_{50}(ER+SRC)$) greater than or equal to 100 nmol/l, and detecting a potency of the physical - chemical interaction of the co-present steroid receptor coactivator-1, and fragments thereof, and the estrogen receptor.

2. (withdrawn) A method of *in vitro* screening for a ligand, said ligand being an estrogen or having estrogenic activity, in a cell-free or enzymatic assay system by selecting a physical-chemical interaction of a co-present steroid receptor coactivator-1, and fragments thereof, and an estrogen receptor, said physical-chemical interaction being measured by detecting a potency of said interaction in the cell-free or enzymatic assay system,

wherein the ligand activates the estrogen receptor and induces said interaction with the co-present steroid receptor coactivator-1, and fragments thereof, in the cell-free or enzymatic assay system with a half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) greater than or equal to 100 nmol/l, and detecting the potency of the physical-chemical interaction of said co-present steroid receptor coactivator-1, and fragments thereof, and of said estrogen receptor.

3. (withdrawn) A method of *in vitro* screening according to claim 2, wherein said ligand is said estrogen and transcriptionally activates a cellular assay system comprising said estrogen receptor and an estrogen-receptor-driven reporter

gene, wherein the ligand activates a potency with a half-maximally effective ligand concentration ($EC_{50}(ER)$) less than or equal to 10 nmol/l.

4.(withdrawn) A method of *in vitro* screening for one or more ligands from a group of test substances, said test substances being selected from the group consisting of estrogens and compounds having estrogen activity, said method comprising the steps of:

a) providing a cell-free or enzymatic assay system for each of said test substances, said cell-free or enzymatic assay system comprising an estrogen receptor for said test substances and a co-present steroid receptor coactivator-1, and fragments thereof.

b) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER+SRC)$) for each of said test substances at which a physical-chemical interaction of said co-present steroid receptor coactivator-1, and said fragments thereof, and said estrogen receptor occurs in the cell-free or enzymatic system in the presence of each of said test substances; and

c) selecting said one or more ligands from said group of test substances if said half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) for said one or more ligands is greater than or equal to 100 nmol/l.

5.(withdrawn) The method as defined in claim 4, wherein said physical-chemical interaction is detected by experimentally measuring fluorescence energy transfer

between a fluorescently-labeled steroid receptor coactivator-1 and a fluorescently-labeled nuclear receptor.

6.(withdrawn) The method as defined in claim 4, wherein said one or more ligands are from said estrogens and transcriptionally activate a cellular assay system at half-maximally effective ligand concentrations less than or equal to 10 nmol/l, wherein said cellular assay system comprises said estrogen receptor and an estrogen-receptor-driven reporter gene.

7.(previously presented) A method of screening a group of test substances for one or more ligands to be administered as effective ingredients in a method of treating neuro-degeneration, said test substances being selected from the group consisting of estrogens and compounds having estrogen activity, said method of screening comprising the steps of:

a) providing a cell-free or enzymatic assay system for each of said test substances, said cell-free or enzymatic assay system comprising an estrogen receptor for said test substances and a co-present steroid receptor coactivator-1, and fragments thereof;

b) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER+SRC)$) for each of said test substances at which a physical-chemical interaction of said co-present steroid receptor coactivator-1, and said fragments thereof, and said estrogen receptor occurs in the cell-free or enzymatic system in the presence of each of said test substances;

c) selecting said one or more of said test substances if said half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) for said one or more of said test substances is greater than or equal to 100 nmol/l;

d) providing a cellular or tissue assay system comprising an estrogen receptor and an estrogen receptor-driven reporter gene;

e) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER)$) for said one or more test substances selected during the selecting of step c) at which said cellular or tissue assay system is transcriptionally activated in the presence of said one or more test substances; and

f) selecting those of said one or more test substances having said half-maximally-effective ligand concentrations that transcriptionally activate said cellular or tissue assay system and that are less than or equal to 10 nmol/l as said one or more ligands for said method of treating said neuro-degeneration.

8.(withdrawn) A method of treating neuro-degeneration in cerebral cortex of a human being, said method comprising the step of administering an effective amount of 3',15 β -dihydrocycloprop[14,15]-estra-1,3,5(10),8-tetraene-3,17 α -diol of said human being.

9.(currently amended) A method of screening a group of test substances for one or more ligands to be administered as effective ingredients in a method of treating neuro-degeneration, said test substances being selected from the group

consisting of estrogens and compounds having estrogen activity, said method of screening comprising the steps of:

a) providing a cell-free or enzymatic assay system for each of said test substances, said cell-free or enzymatic assay system comprising an estrogen receptor for said test substances and a co-present steroid receptor coactivator-1, and fragments thereof;

b) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER+SRC)$) for each of said test substances at which a physical-chemical interaction of said co-present steroid receptor coactivator-1, and said fragments thereof, and said estrogen receptor occurs in the cell-free or enzymatic system in the presence of each of said test substances;

c) selecting said one or more of said test substances if said half-maximally effective ligand concentration ($EC_{50}(ER+SRC)$) for said one or more of said test substances is greater than or equal to 100 nmol/l;

d) providing a cellular or tissue assay system comprising an estrogen receptor and an estrogen receptor-driven reporter gene;

e) experimentally determining half-maximally effective ligand concentrations ($EC_{50}(ER)$) for said one or more test substances selected during the selecting of step c) at which said cellular or tissue assay system is transcriptionally activated in the presence of said one or more test substances; and

f) selecting those of said one or more test substances having said half-maximally-effective ligand concentrations that transcriptionally activate said

cellular or tissue assay system and that are less than or equal to 10 nmol/l as said one or more ligands for said method of treating said neuro-degeneration:

~~The method as defined in claim 7 or 8, wherein~~

wherein said neuro-degeneration is an age-related cognitive disorder, affective disorder, Alzheimer's disease or cerebral ischemia/stroke.